

In the Claims

1. (Cancelled)
2. (Currently Amended) The method according to claim 4 34, wherein the motif or the combination of motifs is a nucleotide or a combination of nucleotides and a subset of sequences is selected from sequences in a databank of nucleic acids.
3. (Currently Amended) The method according to claim 4 34, wherein the motif or the combination of motifs is an amino acid or a combination of amino acids and a subset of sequences is selected from sequences in a databank of polypeptides or proteins.
4. (Currently Amended) The method according to claim 4 34, wherein the reference sequence is a wild-type sequence.
5. (Currently Amended) The method according to claim 4 34, wherein the reference sequence is a sequence comprising in a position i a motif present in position i in a predetermined number of sequences of step (a).
6. (Cancelled)
7. (Currently Amended) The method according to claim 6 34, wherein positions of at least one of the sets E and F are designated by the user.
8. (Currently Amended) The method according to claim 6 34, wherein step (b) further comprises a test step including generating a totality of combinations of possible positions, determining for each of said combinations the value of coefficients R<sub>R</sub> or R<sub>F</sub>, and retaining the combination corresponding to a largest set of positions coefficient R<sub>E</sub> or R<sub>F</sub> of which corresponds to said second value..

9. (Currently Amended) The method according to claim 1 34, wherein the set of sequences comprises sequences of motifs of pathogenic organisms having a high level of mutability.

10. (Currently Amended) The method according to claim 1 34, wherein the set of sequences comprises sequences of motifs of genes implicated in human, animal or plant pathologies having a high level of mutability.

11.-19. (Cancelled)

20. (Currently Amended) The method according to claim 1 34, wherein the set of sequences of step (a) comprises all polypeptide sequences of different variants of a protease of human immunodeficiency virus.

21.-27. (Cancelled)

28. (Currently Amended) The method according to claim 1 34, further comprising, after step (c), a step (e) of comparing motifs identified in step (c) with known drug resistances to observed mutations.

29. (Currently Amended) The method according to claim 1 34, further comprising, after step (c), a step (f) (e) of comparing motifs identified in step (c) with motifs of sequences implicated in at least one of a catalytic site and a site linked by noncompetitive inhibitors.

30.-32. (Cancelled)

33. (Currently Amended) The method of Claim 32 35, wherein the CLUSTAL algorithm is the CLUSTAL W algorithm.

34. (New) A method for identifying a motif or a combination of motifs having a Boolean state of predetermined mutations in a set of sequences comprising:

a) aligning a set of sequences of ordered motifs represented by a single-character code on a programmed computer using a multiple sequence alignment program,

b) comparing a reference sequence with the set of sequences aligned in step (a) by forming a first numerical matrix A of dimensions NxM in which N designates a number of sequences and M designates a number of motifs of one sequence of said alignment, with value  $A_{ij}$  being equal to a first value A1 when the motif of position i of sequence j with a value ranging from 0 to N is mutated in relation to a motif of position i of the reference sequence and equal to a second value A2 in other cases,

forming two analysis matrices B and C of mutations in which:

– matrix B is a matrix of unmutated couples, of couples which do not mutate simultaneously, of dimension MxM, value  $B_{i,k} = B_{k,i}$  being equal:

- to a first value B1 when  $A_{ij} = A_{kj} = A1$  irrespective of the value of j ranging from 0 to N,
- to a second value B2 in other cases;

– matrix C is a matrix of mutated couples of dimension MxM, value  $C_{k,i} = C_{i,k}$  being equal:

- to a second value C1 when  $A_{ij} = A_{kj} = A2$  irrespective of the value of j ranging from 0 to N,
- to a first value C2 in other cases;

determining for a set E of positions a coefficient  $R_E$  whose value is R1 when values  $B_{i,k}$  are equal to a second value B2, irrespective of the values of i and k belonging to set E of said positions,

determining for a set F of positions, a coefficient  $R_F$ , the value of which is R1 when values  $C_{i,k}$  are equal to second value C2, irrespective of the values of i and k belonging to set F of said positions;

wherein in the matrices, i and k designate positions and j designates a sequence, and

c) identifying motifs not having mutated simultaneously or motifs having mutated simultaneously at least once on at least one sequence of the set and not having mutated on another sequence of said set.

35. (New) A method for identifying a motif or a combination of motifs having a Boolean state of predetermined mutations in a set of sequences comprising:

a) aligning a set of sequences of ordered motifs represented by a single-character code on a programmed computer using a CLUSTAL algorithm based multiple sequence alignment program or a Hidden Markov Model algorithm based multiple sequence alignment program,

b) comparing a reference sequence with the set of sequences aligned in step (a) by forming a first numerical matrix A of dimensions NxM in which N designates a number of sequences and M designates a number of motifs of one sequence of said alignment, with value  $A_{ij}$  being equal to a first value A1 when the motif of position i of sequence j with a value ranging from 0 to N is mutated in relation to a motif of position i of the reference sequence and equal to a second value A2 in other cases,

forming two analysis matrices B and C of mutations in which:

– matrix B is a matrix of unmutated couples, of couples which do not mutate simultaneously, of dimension MxM, value  $B_{i,k} = B_{k,i}$  being equal:

- to a first value B1 when  $A_{ij} = A_{kj} = A1$  irrespective of the value of j ranging from 0 to N,
- to a second value B2 in other cases;

– matrix C is a matrix of mutated couples of dimension MxM, value  $C_{k,i} = C_{i,k}$  being equal:

- to a second value C1 when  $A_{ij} = A_{kj} = A1$  irrespective of the value of j ranging from 0 to N,
- to a first value C2 in other cases;

determining for a set E of positions a coefficient  $R_E$  whose value is  $R_1$  when values  $B_{i,k}$  are equal to a second value B2, irrespective of the values of i and k belonging to set E of said positions,

determining for a set F of positions, a coefficient  $R_F$ , the value of which is  $R_1$  when values  $C_{i,k}$  are equal to second value C2, irrespective of the values of i and k belonging to set F of said positions;

wherein in the matrices, i and k designate positions and j designates a sequence, and

c) identifying motifs not having mutated simultaneously or motifs having mutated simultaneously at least once on at least one sequence of the set and not having mutated on another sequence of said set.